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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/599,839

10/11/2006

Marc Chapdelaine

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09/18/2008

ASTRA ZENECA PHARMACEUTICALS LP  
GLOBAL INTELLECTUAL PROPERTY  
1800 CONCORD PIKE  
WILMINGTON, DE 19850-5437

EXAMINER

RAHMANI, NILOOFAR

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

09/18/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/599,839	<b>Applicant(s)</b> CHAPDELAINE ET AL.	
	<b>Examiner</b> NILOOFAR RAHMANI	<b>Art Unit</b> 1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 October 2006.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 7 is/are allowed.
- 6) ☒ Claim(s) 1,2,4-6,8 and 10-17 is/are rejected.
- 7) ☒ Claim(s) 3 and 9 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>02/08/2007</u> .  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. Claims 1-17 are currently pending in the instant application. Claim 18 is cancelled.

2. ***Priority***

This application was filed on 10/11/2006, which is a 371 of PCT/SE05/00500, filed on 04/06/2005, which claims the priority of SWEDEN 0400970-0, filed on 04/14/2004.

3. ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification does not enable the instant compound to activate the  $\alpha 7$  nicotinic receptor and therefore to treat and prevent any and all known or unknown diseases. The claim contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue”. These factors include 1) the breadth of the claims, 2) the nature of the

invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

**The nature of the invention:** The instant invention is drawn to methods and pharmaceutical compositions for treating or preventing a disease or disorder to activate the  $\alpha 7$  nicotinic receptor is beneficial which method comprises administering a therapeutically-effective amount of a compound of formula (I).

**The state of the prior art:** "Genomic clones from the Rdl locus of *Drosophila*, whose mutant phenotype is resistant to cyclodiene insecticides and picrotoxin, were characterized by restriction mapping and partial sequencing to determine intron/exon structure. The coding region of the gene comprises 9 identified exons and span >25 kb of genomic DNA. The structure of the *Drosophila* Rdl receptor subunit was compared with those of vertebrate GABA sub-type A (GABAA)

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receptors and nicotonic acetylcholine receptors (nAChRs). The 1st 6 introns in Rdl show positions similar to those in vertebrate GABAA receptors, whereas the last 2 differ. It is interesting that the last intron appears to be in a position similar to that in nAChRs. These results are examined in relation to the proposal, based on amino acid identities, that Rdl codes for a novel class of GABAA receptor subunit more closely related to glycine receptors, and the possible place of Rdl in the lineage of the receptor superfamily is discussed.” (Ffrench-Constant et al., Journal of Neurochemistry (1992), 59(4), 1562-5).

**The predictability in the art:** It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be useful for treating a pharmacological condition in a subject.

**Amount of guidance/working examples:** Applicant provides no guidance for using a therapeutically effective amount of a compound of Formula (I) could treat any and all known or unknown diseases. Nor does applicant identify what diseases are treatable by therapeutically effective amount of a compound of Formula (I).

**The breadth of the claims:** The breadth of claims is drawn to methods and pharmaceutical compositions for treating or preventing a disease or disorder to activate the  $\alpha 7$  nicotinic receptor is beneficial which method comprises administering a therapeutically-effective amount of a compound of formula (I).

**The quantity of undue experimentation needed:** Since the guidance and teaching provided by the specification is insufficient for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

**The level of the skill in the art:** The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claims 10-17, for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, have been enabled by the instant specification.

4. Further, applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the compounds such as

present here. In addition, it is presumed that “prevention” of the claimed diseases would require a method of identifying those individuals who will develop the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

“The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims”, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before occurs. This would require extensive and potentially opened ended clinical research on healthy subjects. 2) The passage spanning line 5, page 6 to line 33, page 7 lists the diseases Applicant intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to medical treatment and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted before the fact. 6) The artisan using Applicants invention would be a Board Certified physician who specialized to treat diseases with an MD degree and several years of experience.

Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of disorder diseases generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2d 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent disorders generally. That is, the skill is so low that no compound effective generally against disorders has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula (I).

The Examiner suggests deletion of the word "prevention".

**5. Claim Rejections - 35 USC § 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:



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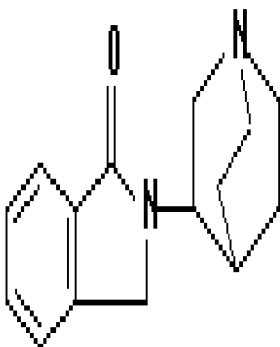
A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2,4-6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Cappelli et al., Bioorganic & Medicinal Chemistry (2002), 10(3), 779-801. Cappelli et al. discloses the instant claimed compound, which from the STN search is

**RN** 431079-01-5

**CN** 1H-Isoindol-1-one, 2-(1-azabicyclo[2.2.2]oct-3-yl)-2,3-dihydro-, hydrochloride



. Therefore, the instant claims are anticipated by Cappelli et al.

## 6. *Claim Objections*

Claims 3, 9 are objected to as being dependent upon a cancelled base claim 1, but would be allowable if rewritten in independent form including all of the limitations of the base claims and any intervening claims.

**7. Allowable Subject Matter**

Claim 7 is patentable over Cappelli et al., Bioorganic & Medicinal Chemistry (2002), 10(3), 779-801. The reference teaches compounds with non-substituted isoindol rings instead of the substituted isoindol ring of the compounds of claim 7. Therefore, the claims are free of prior art.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is 571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/NILOOFAR RAHMANI/

07/24/2008

/D. Margaret Seaman/

Primary Examiner, Art Unit 1625